

AMENDMENTS TO THE CLAIMS

This listing of claims will replace prior versions and listings of claims in the application:

1-29. (Cancelled).

30. (Currently amended) A soluble polypeptide of a the subtilisin-kexin isoenzyme (SKI-1) SKI-1 set forth in SEQ. ID. NO. 6, wherein the soluble polypeptide, ~~the amino acid sequence of which~~ consists of amino acids 187 to 996 of SEQ. ID. NO. 6.

31. (Currently amended) A polypeptide of a the subtilisin-kexin isoenzyme (SKI-1) SKI-1 set forth in SEQ. ID. NO. 6, wherein the soluble polypeptide, ~~the amino acid sequence of which~~ consists of amino acids 17 to 137 of SEQ. ID. NO. 6, which is capable of binding with amino acids 17 to 1052 of SKI-1.

32-35. (Cancelled).

36. (Previously presented) An isolated nucleic acid encoding a polypeptide as defined in claim 30.

37. (Previously presented) An isolated nucleic acid encoding a polypeptide as defined in claim 31.

38-39. (Cancelled).

40. (Previously presented) A recombinant vector comprising the nucleic acid defined in claim 36.

41. (Previously presented) The recombinant vector of claim 40, which is an expression vector.

42. (Previously presented) The recombinant vector of claim 41, which comprises a promoter expressible in a target cell wherein expression of said nucleic acid is desirable.

43. (Previously presented) The recombinant vector of claim 42, which comprises an inducible promoter.

44. (Previously presented) A recombinant host cell comprising the recombinant vector defined in claim 40.

45. (Currently amended) A method of producing ~~a fragment of SKI-1 enzyme~~ the soluble polypeptide of claim 30, which comprises the steps of:

culturing a recombinant host cell expressing a nucleic acid as defined in claim 36 in an expression-supportive culture medium; and recovering ~~said fragment of SKI-1~~ the soluble polypeptide of claim 30 in the culture medium.

46. (Currently amended) A method for cleaving a substrate for a SKI-1 enzyme, which comprises the step of:

contacting said substrate with 1) ~~a polypeptide~~ a soluble fragment of a subtilisin-kexin isoenzyme, the amino acid sequence of which consists consisting of amino acids 187-996 of SEQ. ID. NO. 6; 2) ~~a catalytic part of 1);~~ or 3) ~~a complex as defined in claim 32,~~ for a time sufficient and in conditions adequate for such cleavage to occur, whereby cleavage of the substrate occurs;

with the proviso that said substrate is not a sterol-regulatory element-binding protein (SREBP).

47. (Currently amended) A method for producing a protein or a peptide from a precursor which is an enzymatic substrate for a SKI-1 enzyme, which comprises the steps of:

a) contacting said precursor with 1) ~~a soluble fragment of a subtilisin-kexin isoenzyme, the amino acid sequence of which consists~~ polypeptide consisting of amino acids 187-996 of SEQ. ID. NO. 6; 2) ~~a catalytic part of 1);~~ or 3) ~~a complex as defined in claim 32,~~ for a time sufficient and in conditions adequate for such cleavage to occur; and

b) recovering said protein or peptide;

with the proviso that said substrate is not a sterol-regulatory element-binding protein (SREBP).

48. (Currently amended) The method of claim 47, which takes place in a cell ~~or in the presence of a cellular population~~ and wherein step a) comprises the step of transfecting a cell with a nucleic acid expressing said SKI-1 enzyme.

49. (Previously presented) The method of claim 48, wherein said cell expresses said precursor or is transfected with a nucleic acid expressing said precursor.

50-52. (Cancelled).

53. (Currently amended) A peptide ~~as defined in claim 51~~, which comprises the sequence as set forth in SEQ. ID. NO. 13.

54-55. (Cancelled).

56. (Previously presented) A peptide as defined in claim 53, the amino acid sequence of which consists of the sequence as set forth in SEQ. ID. NO. 14.

57-58. (Cancelled).

59. (Currently amended) A method for screening for a polypeptide ~~that has the activity of having the proteolytic activity of a SKI-1 protease and having an amino acid sequence set forth in SEQ ID NO. 6~~ a subtilisin kexin isoenzyme (SKI-1), the method comprising the steps of:

contacting a peptide capable of binding to and being cleaved by a SKI-1 protease, said peptide comprising an amino acid sequence set forth in any one of SEQ. ID. NOs. 7, 9 and 11, with the proviso that said peptide does not comprise the sequence as set forth in SEQ. ID. NO. 78 and with the proviso that said substrate is not a sterol-regulatory element-binding protein (SREBP), the peptide of claim 51 with a test polypeptide under conditions that allow cleavage of the peptide by the SKI-1 protease having amino acid sequence set forth in SEQ. ID. NO. 6 ~~the SKI-1~~; and

detecting the cleavage of the peptide,

wherein the presence of the cleavage indicates that the polypeptide has SKI-1 proteolytic activity.

60. (Currently amended) A method for monitoring the proteolytic activity of a ~~subtilisin-kexin isoenzyme (SKI-1)~~ SKI-1 protease having amino acid sequence set forth in SEQ. ID. NO. 6, comprising the steps of:

contacting a sample having or suspected of having the proteolytic activity of the SKI-1 protease having amino acid sequence set forth in SEQ. ID. NO. 6 ~~having SKI-1~~ activity with a peptide which is capable of binding to and being cleaved by a SKI-1 protease, said peptide comprising an amino acid sequence set forth in any one of SEQ. ID. NOs. 7, 9 and 11, with the proviso that said peptide does not comprise the sequence as set forth in SEQ. ID. NO. 78 and with the proviso that said substrate is not a sterol-regulatory element-binding protein (SREBP) the peptide of claim 51; and

monitoring the cleavage of the peptide.

61-64. (Cancelled).

65. (Currently amended) A composition comprising a ~~soluble~~ polypeptide ~~of a SKI-1~~ as defined in claim 30.

66. (Cancelled).

67. (Currently amended) A composition comprising a polypeptide of a SK-1 as defined in claim 31.

68-71. (Cancelled).

72. (Previously presented) A composition comprising a nucleic acid as defined in claim 36.

73. (Previously presented) A composition comprising a nucleic acid as defined in claim 37.

74-79. (Cancelled).

80. (Previously presented) A composition comprising a recombinant vector as defined in claim 40.

81. (Previously presented) A composition comprising a recombinant vector as defined in claim 41.

82. (Previously presented) A composition comprising a recombinant vector as defined in claim 42.

83. (Previously presented) A composition comprising a recombinant vector as defined in claim 43.

84-94. (Cancelled).

95. (Currently amended) A purified polypeptide, the amino acid sequence of which consists of amino acids ~~17~~ 18 to 188 of SEQ. ID. NO. 6.

96. (Currently amended) A purified polypeptide, the amino acid sequence of which consists of amino acids ~~17~~ 18 to ~~197~~ 196 of SEQ. ID. NO. 6.

97. (Currently amended) A purified polypeptide, the amino acid sequence of which consists of amino acids ~~17~~ 18 to 169 of SEQ. ID. NO. 6.

98-100.(Cancelled).

101. (Previously presented) An isolated nucleic acid encoding the polypeptide of claim 95.

102. (Previously presented) An isolated nucleic acid encoding the polypeptide of claim 96.

103. (Previously presented) An isolated nucleic acid encoding the polypeptide of claim 97.

104-106. (Cancelled).

107. (Previously presented) A composition comprising the polypeptide of claim 95.

108. (Previously presented) A composition comprising the polypeptide of claim 96.

109. (Previously presented) A composition comprising the polypeptide of claim 97.
- 110-116. (Cancelled).
117. (Previously presented) A recombinant vector comprising the isolated nucleic acid defined in claim 101.
118. (Previously presented) A recombinant vector comprising the isolated nucleic acid defined in claim 102.
119. (Previously presented) A recombinant vector comprising the isolated nucleic acid defined in claim 103.
120. (New) A method as recited in claim 59, wherein said peptide comprises the sequence as set forth in any one of SEQ. ID. NOs. 8, 10 and 12.
121. (New) A method as recited in claim 59, wherein said peptide is labeled.
122. (New) A method as recited in claim 59, wherein said peptide is fluorogenic.
123. (New) A method as recited in claim 59, wherein the amino acid sequence of said peptide is as set forth in SEQ. ID. NO. 14.
124. (New) A method as recited in claim 60, wherein said peptide comprises the sequence as set forth in any one of SEQ. ID. NOs. 8, 10 and 12.
125. (New) A method as recited in claim 60, wherein said peptide is labeled.
126. (New) A method as recited in claim 60, wherein said peptide is fluorogenic.
127. (New) A method as recited in claim 60, wherein the amino acid sequence of said peptide is as set forth in SEQ. ID. NO. 14.